

**IN THE CLAIMS:**

Please amend claims 1, 4, 6, 8-12, 15, 18, 19, 21, 24, 26-30, 33, 36, and 37 as shown in the complete list of claims that is presented below.

1. (Currently Amended) A formulated liposome for incorporating high content of hydrophobic substances comprising:

a first phospholipid, selected from a hydrogenated naturally-occurring phospholipid or a saturated phospholipid with long carbon chains  $-(CH_2)_n-$ , the value of n is at least 14);

a second phospholipid, selected from an unsaturated phospholipid or a saturated phospholipid with short carbon chains  $-(CH_2)_n-$ , the value of n is at most 14) ; one or more hydrophobic substances; and

liposome-forming materials,

wherein the first and the second phospholipid coexist in the liposome in two immiscible phases and create several discontinuous regions, and a molar ratio of the first phospholipid to the second phospholipid is larger than 1/20; a phase transition temperature  $T_{g1}$  of the first phospholipid is in the range between 40 and 70 74 °C, and a phase transition temperature  $T_{g2}$  of the second phospholipid is in the range between -30 and 10 °C while a drug delivery temperature  $T_1$  and a drug storage temperature  $T_2$  are chosen at specified ranges subject to an order of  $T_{g1} > T_1 > T_2 > T_{g2}$ . The two immiscible phases coexist in the liposome and create several discontinuous regions.

2. (Original) The liposome according to claim 1, wherein the phase transition temperature of the first phospholipid is preferably in the range between 50 and 65 °C, and the phase transition temperature of the second phospholipid is preferably in the range between -20 and 4 °C.

3. (Original) The liposome according to claim 1, wherein the first phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

4. (Currently Amended) The liposome according to claim 3, wherein phospholipid is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearoyl phosphatidyl choline (DSPC), diarachidoyl phosphatidyl choline, dimyristoyl phosphatidyl ethanolamine (DMPE), dipalmitoyl phosphatidyl ethanolamine (DPPE), distearoyl phosphatidyl ethanolamine (DSPE), ~~diarachidoyl phosphatidyl ethanolamine~~, dipalmitoyl phosphatidyl glycerol (DPPG), distearoyl phosphatidyl glycerol, dimyristoyl phosphatidyl acid (DMPA), dipalmitoyl phosphatidyl acid (DPPA), dipalmitoyl phosphatidyl serine (DPPS), and distearoyl phosphatidyl serine (DSPS).

5. (Original) The liposome according to claim 1, wherein the second phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol

(PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

6. (Currently Amended) The liposome according to claim 5, wherein phospholipid is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, dipetroselinoyl phosphatidyl choline, dipalmitaidoyl phosphatidyl choline, ~~dipalmitoleoyl phosphatidyl choline, dipalmitaidoyl phosphatidyl ethanolamine~~, dioleoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl serine, dilauroyl phosphatidyl choline (DLPC), diundecanoyl phosphatidyl choline, ~~didecanoyl phosphatidyl choline, dinonanoyl phosphatidyl choline~~, didecanoyl phosphatidyl ethanolamine, and dinonanoyl phosphatidyl ethanolamine.

7. (Original) The liposome according to claim 1, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

8. (Currently Amended) The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is paclitaxel and/or docetaxel - a derivative thereof.

9. (Currently Amended) The liposome according to claim 8, wherein paclitaxel and/or docetaxel the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 25 mole%.

10. (Currently Amended) The liposome according to claim 9, wherein paclitaxel and/or docetaxel ~~the derivative thereof~~ are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

11. (Currently Amended) The liposome according to claim 9, wherein paclitaxel and/or docetaxel ~~the derivative thereof~~ are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

12. (Currently Amended) The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is retinoic acid and/or a derivative thereof, the retinoic acid derivatives include retinol, retinyl acylate and retinyl acetate.

13. (Original) The liposome according to claim 12, wherein the retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 40 mole%.

14. (Original) The liposome according to claim 13, wherein retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 10

mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

15. (Currently Amended) The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is camptothecin and/or a derivative thereof, wherein the derivatives of camptothecin include irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

16. (Original) The liposome according to claim 15, wherein the camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 30 mole%.

17. (Original) The liposome according to claim 16, wherein camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

18. (Currently Amended) The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is selected from the group consisting of paclitaxel and/or a derivatives thereof, retinoic acid and/or the derivatives thereof, and camptothecin and/or the derivatives thereof, wherein the derivative of paclitaxel includes docetaxel; the derivatives of retinoic acid include retinol, retinyl acylate and retinyl acetate; the derivatives of camptothecin include irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

19. (Currently Amended) The liposome according to claim 1, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, cholesterol derivative derivatives, antioxidant, and mixtures thereof, wherein cholesterol derivatives include polyethylene glycol 600 mono(cholesteryl) ether sebacate and cholesteryl oleyl carbonate.

20. (Original) The liposome according to claim 19, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearylloyl phosphatidyl ethanolamine (MPEG-DSPE).

21. (Currently Amended) A The liposome for incorporating high content of hydrophobic substances comprising:

a first phosphatidyl choline, selected from a hydrogenated naturally-occurring phospholipid or a saturated phospholipid with long carbon chains  $-(CH_2)_n-$ , the value of n is at least 14);

a second phosphatidyl choline, selected from an unsaturated phospholipid or a saturated phospholipid with short carbon chains  $-(CH_2)_n-$ , the value of n is at most 14); one or more hydrophobic substances; and

liposome-forming materials,

wherein the first and the second phosphatidyl cholines coexist in the liposome in two immiscible phases and create several discontinuous regions, and a molar ratio of the first phosphatidyl choline to the second phosphatidyl choline is larger than 1/20; a phase transition temperature  $T_{g1}$  of the first phospholipid phosphatidyl choline is in the range between 40 and 70 74 °C and a phase transition temperature  $T_{g2}$  of the second phospholipid phosphatidyl choline is in the range between –30 and 10 °C, and a drug delivery temperature T<sub>1</sub> and a drug storage temperature T<sub>2</sub> are chosen at specified ranges subject to an order of T<sub>g1</sub> > T<sub>1</sub> > T<sub>2</sub> > T<sub>g2</sub>.

22. (Original) The liposome according to claim 21, wherein the phase transition temperature of the first phospholipid is preferably in the range from 50 to 65 °C, and the phase transition temperature of the second phospholipid is preferably in the range from –20 to 4 °C.

23. (Original) The liposome according to claim 21, wherein the first phosphatidyl choline (PC) is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearoyl phosphatidyl choline (DSPC),

24. (Currently Amended) The liposome according to claim 21, wherein the second phosphatidyl choline is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), synthetic or natural-occurring unsaturated phosphatidyl cholines and dilauroyl phosphatidyl choline (DLPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, and dipetroselinoyl phosphatidyl choline, dipalmitelaidoyl phosphatidyl choline, ~~and~~ ~~dipalmitoleoyl phosphatidyl choline.~~

25. (Original) The liposome according to claim 21, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

26. (Currently Amended) The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is paclitaxel and/or docetaxel a derivative thereof.

27. (Currently Amended) The liposome according to claim 26, wherein the paclitaxel and/or docetaxel its derivative is are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 25 mole%.

28. (Currently Amended) The liposome according to claim 27, wherein paclitaxel and/or docetaxel the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

29. (Currently Amended) The liposome according to claim 27, wherein paclitaxel and/or docetaxel the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

30. (Currently Amended) The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is retinoic acid and/or a derivative thereof, the retinoic acid derivatives include retinol, retinyl acylate and retinyl acetate.

31. (Original) The liposome according to claim 30, wherein the retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 40 mole%.

32. (Original) The liposome according to claim 31, wherein retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 10

mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

33. (Currently Amended) The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is camptothecin and/or a derivative, and the derivatives of camptothecin include irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

34. (Original) The liposome according to claim 33, wherein the camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 30 mole%.

35. (Original) The liposome according to claim 34, wherein camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

36. (Currently Amended) The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is selected from the group consisting of paclitaxel, retinoic acid, camptothecin and the derivatives thereof, wherein the derivative of paclitaxel includes docetaxel; the derivatives of retinoic acid include retinol, retinyl acylate and retinyl acetate; the derivatives of camptothecin include irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

37. (Currently Amended) The liposome according to claim 21, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, cholesterol derivative derivatives, antioxidant, and mixture thereof, wherein cholesterol derivatives include polyethylene glycol 600 mono(cholesteryl) ether sebacate and cholesteryl oleyl carbonate.

38. (Original) The liposome according to claim 37, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).